

a1
cont

underlining indicates the two sequences that served to design degenerate oligonucleotides for PCR. The first occurrence of thick underlining is directed to mink kip1 and mouse kip1 sequence NLFGPVNHEELTR (SEQ ID NO: 26) and human kip1 sequence NLFGPVDHEELTR (SEQ ID NO: 27). The sequence LFGPVN (SEQ ID NO: 22) within NLFGPVNHEELTR and the sequence LFGPVD (SEQ ID NO: 25) within NLFGPVDHEELTR respectively correspond to the longest uninterrupted stretch of identity to Cip1/WAF1 (SEQ ID NO: 24). B, Sequence alignment between human Kipl and Cip1/WAFT. The putative bipartite nuclear localization signal in both proteins is underlined. A Cdc2 kinase consensus site present in Kipl is indicated by a thick bar.

On page 17, please replace the paragraph starting at line 25 with:

a2
Mink Kipl cDNA and the encoded mink kip1 (SEQ ID NOs: 5 and 6).

On page 17, please replace the paragraph starting at line 28 with:

a3
Mouse Kibl cDNA and the encoded mouse kip1 (SEQ ID NOs: 3 and 4).

On page 17, please replace the paragraph at line 31 with:

a4
Human Kipl cDNA and the encoded human kip1 (SEQ ID NOs: 1 and 2).

On page 18, please replace the paragraphs from line 32 to line 40 (inside Table I) with:

- a5
1. Asn-Leu-Tyr-Pro-Leu-Thr-Asn-Tyr-Thr-Phe (SEQ ID NO: 7)
 2. Thr-Asp-Thr-Ala-Asp-Asn-Gln-Ala-Gly-Leu-Ala-Glu-Gln (SEQ ID NO: 8)
 3. Gln-Ala-Val-Pro-Leu-Met-Gly-Pro-Gln-Glu (SEQ ID NO: 9)
 4. Leu-Pro-Glu-Phe-Tyr-Tyr-Arg-Pro-Pro-Arg-Pro-Pro (SEQ ID NO: 10)
 5. Tyr-Glu-Trp-Gln-Glu-Val (SEQ ID NO: 11)

On page 39, please replace the paragraphs from line 28 to line 32 with:

- 17
1. Asn-Leu-Tyr-Pro-Leu-Thr-Asn-Tyr-Thr-Phe (SEQ ID NO: 7)
 2. Thr-Asp-Thr-Ala-Asp-Asn-Gln-Ala-Gly-Leu-Ala-Glu-Gln (SEQ ID NO: 8)
 3. Gln-Ala-Val-Pro-Leu-Met-Gly-Pro-Gln-Glu (SEQ ID NO: 9)
 4. Leu-Pro-Glu-Phe-Tyr-Tyr-Arg-Pro-Pro-Arg-Pro-Pro (SEQ ID NO: 10)

5. Tyr-Glu-Trp-Gln-Glu-Val (SEQ ID NO: 11)

On page 40, please replace the paragraphs from line 8 to line 45 (inside Table II) with:

Peptide #1: None

Peptide #2:

Sense 5' -AC (N) -GA (T/C) -AC (N) -GA (T/C) -AA (T/C) -
CA (A/G) -GC-3' (SEQ ID NO: 12)

Antisense 5' - (N) GC- (T/C) TG- (A/G) TT- (A/G) TC- (N) GC -
(N) GT-(A/G) TC- (N) GT-3' (SEQ ID NO: 13)

Peptide #3:

Sense 5' -CA (A/G) -GC (N) -GT (N) -CC (N) -CT (N) -ATG-GG-3'
(SEQ ID NO: 14)

and 5' -CA (A/G) -GC (N) -GT (N) -CC (N) -TT (A/G) -ATG -
GG-3' (SEQ ID NO: 15)

Antisense 5' - (N) CC-CAT- (N) AG- (N) GG- (N) AC- (N) GC -
(T/C)TG-3' (SEQ ID NO: 16)

and 5' - (N) CC-CAT- (T/C) AA- (N) GG- (N) AC- (N) GC -
(T/C) TG-3' (SEQ ID NO: 17)

Peptide #4:

Sense 5' -CC (N) -GA (A/G) -TT (T/C) -TA (T/C) -TA (T/C) -
(C/A)G-3' (SEQ ID NO: 18)

Antisense 5' -C (T/G) - (A/G) TA- (A/G) TA- (A/G) AA- (T/C) TC -
(N) GG-3' (SEQ ID NO: 19)

Peptide #5:

Sense 5' -TA (T/C) -GA (A/G) -TGG-CA (A/G) -GA (A/G) -GT -3'
(SEQ ID NO: 20)

Antisense 5' - (N) AC- (T/C) TC- (T/C) TG-CCA- (T/C) TC-
(A/G) TA-3' (SEQ ID NO: 21)

On page 71, please replace the paragraph starting at line 23 with:

a⁸
The Kipl region that is similar to Cip1/WAFT is sufficient to inhibit Cdk activity when tested as a 52- amino acid peptide in vitro. This 52 amino acid segment contains the sequence LFGPVN (SEQ ID NO: 22) which corresponds to the longest un-interrupted stretch of identity to Cip1/WAF1 and, interestingly, is similar to the FAR1 sequence LSQPVN (SEQ ID NO: 23) located in a region required for interaction with CLN2-CDC28 (Peter et al., 1993).

The paragraphs presented above incorporate changes as indicated by the marked-up versions below.

Page 16, the paragraph starting at line 7:

Mammalian Kip1 sequences, and comparison with Cip1/WAF1. A, Amino acid sequences deduced from Kip1 cDNAs from mink (mk), mouse (m) and human (h). Identical amino acids are indicated by dots. The available mink sequence is incomplete at the C-terminus. Peptide sequences obtained from purified Kip1 are underlined. Thick underlining indicates the two sequences that served to design degenerate oligonucleotides for PCR. The first occurrence of thick underlining is directed to mink kip1 and mouse kip1 sequence NLFGPVNHEELTR (SEQ ID NO: 26) and human kip1 sequence NLFGPVDHEELTR (SEQ ID NO: 27). The sequence LFGPVN (SEQ ID NO: 22) within NLFGPVNHEELTR and the sequence LFGPVD (SEQ ID NO: 25) within NLFGPVDHEELTR respectively correspond to the longest uninterrupted stretch of identity to Cip1/WAF1 (SEQ ID NO: 24). B, Sequence alignment between human Kip1 and Cip1/WAFT. The putative bipartite nuclear localization signal in both proteins is underlined. A Cdc2 kinase consensus site present in Kip1 is indicated by a thick bar.

Page 17, the paragraph starting at line 25:

Mink Kip1 cDNA and the encoded mink kip1 (SEQ ID NOs: 5 and 6).

Page 17, the paragraph starting at line 28:

Mouse Kip1 cDNA and the encoded mouse kip1 (SEQ ID NOs: 3 and 4).

Page 17, the paragraph at line 31:

Human Kipl cDNA and the encoded human kipl (SEQ ID NOs: 1 and 2).

Page 18, the paragraphs from line 32 to line 40 (inside Table I):

1. Asn-Leu-Tyr-Pro-Leu-Thr-Asn-Tyr-Thr-Phe (SEQ ID NO: 7)
2. Thr-Asp-Thr-Ala-Asp-Asn-Gln-Ala-Gly-Leu-Ala-Glu-Gln (SEQ ID NO: 8)
3. Gln-Ala-Val-Pro-Leu-Met-Gly-Pro-Gln-Glu (SEQ ID NO: 9)
4. Leu-Pro-Glu-Phe-Tyr-Tyr-Arg-Pro-Pro-Arg-Pro-Pro (SEQ ID NO: 10)
5. Tyr-Glu-Trp-Gln-Glu-Val (SEQ ID NO: 11)

Page 39, the paragraphs from line 28 to line 32:

1. Asn-Leu-Tyr-Pro-Leu-Thr-Asn-Tyr-Thr-Phe (SEQ ID NO: 7)
2. Thr-Asp-Thr-Ala-Asp-Asn-Gln-Ala-Gly-Leu-Ala-Glu-Gln (SEQ ID NO: 8)
3. Gln-Ala-Val-Pro-Leu-Met-Gly-Pro-Gln-Glu (SEQ ID NO: 9)
4. Leu-Pro-Glu-Phe-Tyr-Tyr-Arg-Pro-Pro-Arg-Pro-Pro (SEQ ID NO: 10)
5. Tyr-Glu-Trp-Gln-Glu-Val (SEQ ID NO: 11)

Page 40, the paragraphs from line 8 to line 45 (inside Table II):

Peptide #1: None

Peptide #2:

Sense 5' -AC (N) -GA (T/C) -AC (N) -GA (T/C) -AA (T/C) -
CA (A/G) -GC-3' (SEQ ID NO: 12)

Antisense 5' - (N) GC- (T/C) TG- (A/G) TT- (A/G) TC- (N) GC -
(N) GT-(A/G) TC- (N) GT-3' (SEQ ID NO: 13)

Peptide #3:

Sense 5' -CA (A/G) -GC (N) -GT (N) -CC (N) -CT (N) -ATG-GG-3'
(SEQ ID NO: 14)

and 5' -CA (A/G) -GC (N) -GT (N) -CC (N) -TT (A/G) -ATG -
GG-3' (SEQ ID NO: 15)

Antisense 5' - (N) CC-CAT- (N) AG- (N) GG- (N) AC- (N) GC -
(T/C)TG-3' (SEQ ID NO: 16)

and 5' - (N) CC-CAT- (T/C) AA- (N) GG- (N) AC- (N) GC -
(T/C) TG-3' (SEQ ID NO: 17)

Peptide #4:

Sense 5' -CC (N) -GA (A/G) -TT (T/C) -TA (T/C) -TA (T/C) -
(C/A)G-3' (SEQ ID NO: 18)

Antisense 5' -C (T/G) - (A/G) TA- (A/G) TA- (A/G) AA- (T/C) TC -
(N) GG-3' (SEQ ID NO: 19)

Peptide #5:

Sense 5' -TA (T/C) -GA (A/G) -TGG-CA (A/G) -GA (A/G) -GT -3'
(SEQ ID NO: 20)

Antisense 5' - (N) AC- (T/C) TC- (T/C) TG-CCA- (T/C) TC-
(A/G) TA-3' (SEQ ID NO: 21)

Page 71, the paragraph starting at line 23:

The Kipl region that is similar to Cip1/WAFT is sufficient to inhibit Cdk activity when tested as a 52- amino acid peptide in vitro. This 52 amino acid segment contains the sequence LFGPVN (SEQ ID NO: 22) which corresponds to the longest un-interrupted stretch of identity to Cip1/WAF1 and, interestingly, is similar to the FAR1 sequence LSQPVN (SEQ ID NO: 23) located in a region required for interaction with CLN2-CDC28 (Peter et al., 1993).

In the claims:

For the convenience of the Examiner, the pending claims of Groups IV and VI, whether or not amended, are presented below.

23. (**Amended**) A method of treating a subject having a hyperproliferative disorder which comprises administering to the subject a therapeutically effective amount of an agent capable of specifically enhancing the ability of a p27 protein comprising a sequence at least 90% identical to amino acid residues 28-88 of SEQ ID NO: 2 to inhibit the